



Antimicrobial Activities of Nanoparticles: Mechanisms of Action and Biomedical Applications

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ABSTRACT

Nanoparticles (NP) have emerged as a versatile source of an antimicrobial substance that is known to be efficient against viruses, protozoa, fungi and bacteria. Their size dependence, which is unique, and the high surface-area-to-volume ratio and tuneable surface chemistry make the antimicrobial peptides interactive with microbial cells along a different mechanism in comparison to classical antibiotics. The review will combine the existing information on the mechanism of action of nanoparticles as antimicrobial agent, give the overview of various major classes of nanoparticles (metallic, metal oxide nuclei, polymeric, lipid based and hybrid systems), and discusses previous and possible biomedical applications. A special focus is being done on mechanistic pathways through membrane disruption, generation of reactive oxygen species (ROS), release of metal ions, interaction with intracellular targets and anti-biofilm activity. The review is also concerned with methodological concerns in antimicrobial testing, in vivo and translational innovations; wound dressings, implant overcoats, drug delivery vehicles, diagnostic platforms and addresses seriously safety, resistance progeny and regulatory concerns. Conclusively, future directions are also given that will ensure the safety of the research towards clinical translation, and it will be less harmful in terms of environmental and toxicological risks.

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INTRODUCTION

Nanotechnology has transformed numerous fields of science and industry and afforded novel chances of accommodation, drug delivery, and drug administration (Saeed et al. 2025). The transference of nanoparticles (NPs) having excellent antimicrobial promises is among its best bets (Wahab et al. 2023). With engineered materials of less than 100 nanometers, nanoparticles have unique physical, chemical and biological characteristics (Joudeh and Linke 2022). This size enhances the surface-to-volume ratio of these materials by enormous amounts, and this yields increased reactivity and tunable surface behaviour, and size-dependent optical, electrical and

catalytic properties (Jašik et al. 2022). The interaction of NPs with microbial membranes, permeation into biofilm and interference with intracellular processes is because of these properties (Lahiri et al. 2021). The last two decades have shown that Nano-materials have tremendous antimicrobial properties against diverse pathogens, including multi-drug-resistant pathogens and opportunistic fungi; nanoparticles found include silver or zinc oxide nanoparticles, titanium dioxide and chitosan nanoparticles (Mba and Nweze 2021). These Nano-scale agents are increasingly finding a biological route to wound dressings, implant coating, textiles and targeted drug carriers demonstrating their growing biomedical significance (Harish et al. 2022).

The above promising developments would not eliminate the fact that the increasing prevalence of antimicrobial resistance (AMR) practice has turned into a threat to global health and has rendered some conventional antibiotics useless as well. The World Health Organization (WHO) has said that unless other approaches are formulated, AMR will take a toll of as many as 10 million lives annually by 2050 (Ferraz 2024). AMR presents a compounded problem with the reporter on the low speed of developing and using new antibiotics and misusing drugs that are in use (Qureshi et al. 2023). The traditional antimicrobials are normally anticipated to influence a particular cellular pathway, and microorganisms can circumvent these pathways using genetic mutation or efflux (Abbas et al. 2025). Conversely, the multifaceted action occurring of nanoparticles via oxidative stress models to membrane disruption makes it less likely to develop resistance (Shaikh et al. 2019). Nevertheless, there are obstacles to nanoparticle biosafety, potential cytotoxicity of biofilms to the host tissues, environmental accumulation and the standardization of testing method (Kus-Liśkiewicz et al. 2021). Moreover, understanding the finer physical mode of action that conceptualizes their antimicrobial action is essential in the development of safer and more effective nanomaterials as a clinical application (Sadiq et al. 2023).

The aim of this review is to present a detailed account of antimicrobial activities of nanoparticles, especially mechanistic relationships and different biomedical applications. Specifically, this manuscript (1) describes the physicochemical properties of representative nanoparticle classes of antimicrobial activity; (2) clarifies their mechanisms of action regarding microbial cells (e.g., membrane rupture, ROS, metal ion delivery and inhibition of biofilm); (3) review recent advances in clinical uses of nanoparticle-wound healing, drug delivery, implants and diagnostics; and (4) emerging toxicity, resistance and regulatory considerations. This review will consolidate existing knowledge about the great therapeutic promise of nanoparticles and the scientific and ethical challenges in putting them in the antimicrobial arsenal.

Classification and physicochemical features of nanoparticles

Nanoparticles that are employed for antimicrobial applications consist of a wide variety of materials and architectures (Ortega-Nieto et al. 2023). Metallic nanoparticles (silver, round spheres, Ag), (gold, a little bell-shaped, Au) and copper (Cu), (zinc, Zn) and metal oxide nanoparticle of interest are those of zinc oxide (ZnO) and titanium dioxide (TiO₂) and have been most investigate for intrinsic microbicidal (Harish et al. 2022). Polymeric nanoparticles (chitosan or synthetic polymers, etc.) can exert antimicrobial activity through the effect of cationic surface charge and can be used as carriers for antibiotics or antiseptics (Parcheta and Sobiesiak 2023). Lipid-based systems (e.g. liposomes, solid lipid nanoparticles) allow encapsulation and targeted delivery of antimicrobial agents (Ranjbar et al. 2023). Hybrid and composite nanoparticles combine two or more materials in such a way to make use of complementary mechanisms (Wang et al. 2024). Key physicochemical properties that determine antimicrobial efficacy are particle size, shape, surface area, surface charge, zeta potential, crystallinity,

and aggregation state (Menichetti et al. 2023). Smaller nanoparticles are more easily able to cross biological barriers and have higher reactivity, but size-dependent considerations regarding toxicity and bio-distribution need to be taken into account in biomedical applications (Abbasi et al. 2023; Khan et al. 2025).

Mechanisms of antimicrobial action

One of the several mechanisms that nanoparticles find themselves acting is multi-mechanistic. They are processes that we need to comprehend under the circumstances of reasonable architecture and risk-free point-of-use (Jafarbeigi and Martyushev 2025; Pollini et al. 2025). One of the main forms of membrane interaction with molecules and physical disruption (Zhao et al. 2024). Lots of nanoparticles on the surface of microbial cells settle through electrostatic force, especially cationic NPs in contact with anionic materials of such bacterial cell walls and fungal membrane systems of cells debasing the membranes (Modi et al. 2023). The leakage of cytoplasmic contents and cell death are caused by physical puncture, augmented permeability, and lipid peroxidation (Zheng et al. 2024). Distinctive shapes, e.g., acute-edged or rod-similar NPs, raise disruption by mechanical means (Zare et al. 2021).

Another prevalent mechanism is the production of reactive oxygen species (ROS), especially when photocatalytic metal oxides such as TiO₂ and ZnO are involved (Raub et al. 2024; Senthil Rathil et al. 2024). These materials generate hydroxyl radicals, superoxide anions, and hydrogen peroxide under the proper excitation (e.g., to create doped systems, using UV or visible light) (Peter et al. 2024). They affect ROS attack proteins, lipids, and nucleic acids, which produce oxidative stress because antioxidant defences of microorganisms could not withstand it (Sahu et al. 2022).

Releasing of metal ions facilitates antimicrobial properties in metallic and metal oxide nanoparticles (Hosseinizadeh 2025). Ag, Cu, or Zn ion dissolution in an aqueous medium can lead to this solution of the ions disrupting vital enzyme activities, membrane destabilization, and thiol group binding in proteins (Tiwari et al. 2025). The kinetics of release of ions depends on the composition, size as well as the milieu of the particle; in design-controlled release the milieu is designed to maintain antimicrobial levels whilst avoiding systemic exposure (Cheng et al. 2025).

Binding to intracellular targets is achieved through direct binding with DNA, ribosomes, disrupting electron transport chains, and binding inhibiting enzymatic pathways (Zhang et al. 2024). Nanoparticles or released ions may destabilize the ATP production and signal transduction, hence metabolic collapse (Qu et al. 2023). The mechanism that results in anti-biofilm activity is that nanoparticles can penetrate extracellular polymeric substances as well as prevent biofilm formation, or the ability to disrupt existing biofilm (Mohanta et al. 2023). Other NPs disable quorum sensing pathways or deactivate by enzymatic, break down queue of the matrix, making bacteria more prone to antimicrobials (Juszczuk-Kubiak 2024) (Fig 1). Synergistic and combined mechanisms are frequently observed: a nanoparticle may simultaneously generate ROS, release ions, and mechanically stress

Mechanisms of resistance and antimicrobial activity

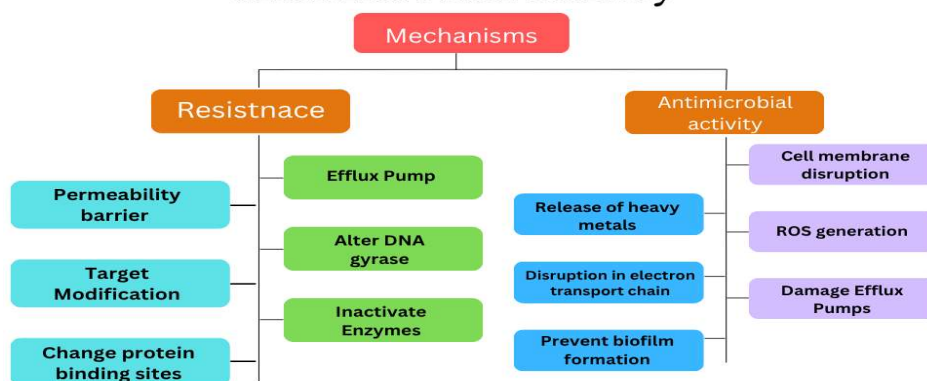


Fig 1: Mechanisms of antimicrobial resistance and antimicrobial activity of nanoparticles.

membranes (Zhang et al. 2025a). This multimodal action is advantageous for overcoming single-target resistance mechanisms.

Major nanoparticle types their antimicrobial efficacy

Ag-NPs have continued to be the most widely researched antimicrobial NPs (Bamal et al. 2021). Ag-NPs have broad-spectrum activity in gram-positive and gram-negative bacteria, fungi and some viruses (Alavi and Ashengroph 2023). Their versatile activity, including membrane interaction, release of ions (Ag^+) and association with the intracellular components, explains strong antimicrobial actions of very low concentrations (Petcu et al. 2024). Nevertheless, the cytotoxicity issue, environmental build-up and development of silver resistance in some situations, trigger cautious optimization (Duman et al. 2024) (Table 1).

Au-NPs are also less intrinsically antimicrobial but useful in: photo-thermal therapy, surface-enhancing antimicrobial delivery and diagnostics (Tian et al. 2024). Antimicrobial peptides or antibiotics conjugated to functionalized equally facile killing through targeted delivery and local photo-thermal heating with the near-infrared intense light (Zhang et al. 2025b). Copper and copper oxide nanoparticles have high antimicrobial capability and are more appealing to low end markets like surface finishes (Omar et al. 2024). Copper ions interfere with the membranes and proteins and have the ability to produce ROS (Sun et al. 2022). But the toxicity of copper makes copper require use within biomedical parameters (Crisan et al. 2021).

TiO₂ (titanium oxide) and ZnO nanoparticles represent themselves through the actions of ROS formation and release of zinc (and titanium) ions (ZnO) (Wen et al. 2023). Visible-light-activated photo catalytic doped TiO₂ has been applied to antimicrobial coating and water treatment (Schutte-Smith et al. 2023). ZnO is valued at appropriate dosage levels for its excellent wound-healing properties (Pino et al. 2023). Chitosan-derived nanoparticles utilize the native property of chitosan to act as cationic and mucoadhesive nano-systems and provide antimicrobial properties and drug delivery with an overall propitious biocompatibility (Abu-Elala et al. 2025). Polymeric NP can also be designed to deliver antibiotics slowly and to be specific to intracellular pathogens (Le et al. 2021).

Nanoparticles made of lipids, like liposomes, offer biocompatible nanoparticles that entrap antibiotics, antiviral drugs, antifungals, or antiviral drugs and have an improved pharmacokinetic profile and reduce off-target toxicity (Georgakopoulou et al. 2024). The antimicrobials and vaccines have experimental clinical success with liquids (Frost et al. 2023). Examples of hybrids and composite NPs include silver-decorated polymeric matrices, metal-metal oxide composite, multifunctional Nano shells, which incorporate antimicrobial potency with specific release and surface characteristics that can be used in implants and other devices (Lee et al. 2017).

Methods for evaluating antimicrobial activity of nanoparticles

A strong evaluation of NP antimicrobial efficacy necessitates supplemental in vitro and in vivo procedures and nanoparticle-specific artefacts that will be considered (Rezić and Meštrović 2023). Adapted tests related to antibiotic tests to include minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), time-kill and disk diffusion and biofilm as standard assays are still a useful tool, though can be confounded by nanoparticle aggregation, adsorption to biological media and light-instigating activity in case of photo-catalyst NPs (Bento et al. 2021; Franconi and Lupetti 2023). Coupled with biological measurements, physicochemical characterization should be too: dissemination of particles size, zeta potential, fashion of dissolution/ion release, surface chemistry, aggregation nation under experiment conditions should be provided (Pérez et al. 2023; Vela et al. 2023).

Mechanistic information is provided by advanced microscopy (scanning and transmission electron microscopy), membrane integrity and ROS fluorescence corresponding assays, proteomics and trans-cryptomics (He et al. 2021). Those in vivo models of infection and biocompatibility, including wound infection models, implant-associated infection models and systemic toxicity models, are essential in the process of translational evaluation (Frisch et al. 2023). Standardization of protocols and reporting is a topic that has continued to require standardization in an effort to provide comparative trials and move forward in efforts of clinical translation (Hawthorne 2024).

Table 1: Types of nanoparticles targeting multiple microorganisms and their mechanisms of action

Nanoparticle Type	Composition / Example	Primary Mechanism of Action	Target Microorganisms	Biomedical Applications	Advantages	Limitations	References
Silver (Ag-NPs)	Elemental silver nanoparticles	Disruption of cell membrane, ROS generation, Ag ⁺ ion release	Broad-spectrum: Gram-positive, Gram-negative bacteria, fungi, some viruses	Wound dressings, catheters, implant coatings	High antimicrobial potency, broad spectrum	Cytotoxicity, environmental accumulation, potential resistance	(Rodrigues et al. 2024)
Gold (Au-NPs)	Elemental gold nanoparticles	Surface fractionalization for targeted delivery, photo-thermal killing	Bacteria and fungi (via conjugated systems)	photo-thermal therapy, bio-sensing, antimicrobial coatings	Biocompatibility, ease of surface modification	Weak intrinsic antimicrobial effect, high cost	(Alavi et al. 2022)
Copper (Cu-NPs)	Metallic or oxide copper	Cu ⁺ /Cu ²⁺ ion release, ROS generation, protein oxidation	Bacteria, fungi, viruses	Surface coatings, textiles, dental materials	Cost-effective, strong antimicrobial	Cytotoxicity, oxidative stress to host cells	(Solangi et al. 2024)
Zinc oxide (ZnO NPs)	ZnO nanoparticles	ROS generation, Zn ²⁺ ion release	Bacteria and fungi	Wound healing, drug delivery, dental composites	Biocompatibility, UV-activated antibacterial	Photoactivation needed, toxicity at high doses	(Murali et al. 2023)
Titanium Dioxide (TiO ₂ NPs)	TiO ₂ (anatase, rutile)	Photocatalytic ROS generation	Bacteria and viruses	Surface disinfectants, implants, coatings	Stability, self-cleaning properties	Requires UV/visible activation, limited in dark	(Ghareeb et al. 2024)
Chitosan NPs	Chitosan polymer-based	Electrostatic membrane disruption, chelation of metals	Bacteria, fungi	Wound dressings, drug carriers	Biodegradable, low toxicity	Limited stability at neutral pH	(Mostafa et al. 2022)
Polymeric NPs	PLGA, PEG, PCL-based systems	Sustained drug release, encapsulated antimicrobial action	Bacteria and intracellular pathogens	Antibiotic delivery, biofilm penetration	Controlled release, versatility	Limited intrinsic antimicrobial action	(Aguilera-Correa et al. 2021)
Lipid-based NPs	Liposomes, SLNs, NLCs	Encapsulation of antibiotics, fusion with cell membranes	Bacteria, fungi	Drug delivery, vaccine adjuvants	Biocompatibility, targeted delivery	Physical instability, oxidation	(Upare et al. 2025)
Hybrid/Composite NPs	Ag–ZnO, Au–TiO ₂ , polymer–metal composites	Combined ROS and ion release, synergistic action	Bacteria, fungi, biofilms	Implants, wound healing, coatings	Multifunctional, synergistic antimicrobial	Complex synthesis, regulatory challenges	(Eltarhony et al. 2021)

Biomedical applications and translational progress

There have been pursuits of nanoparticle antimicrobials in various fields of biomedical application (Jangid et al. 2024). As an antimicrobial agent, silver nanoparticles have found medically beneficial applications to wound care: dressings impregnated with silver nanoparticles offer antimicrobial protection, and scaffolds made of chitosan offer antimicrobial protection together with tissue reconstruction (Zhou et al. 2021; Nicolae-Maranciuc and Chicea 2025). Antimicrobial NPs created on the surfaces of implantable devices as anti-infectious layers are expected to eliminate device-associated infections in orthopedics, dentistry, and cardiology this way, by providing a hostile environment in which microorganisms are not able to colonize (Hudiță et al. 2022; Mercan et al. 2022). Application to drug delivery is high-potency One way of using nanoparticles in food

production is chemical drug delivery (Mohamed-Ezzat et al. 2025). The antennal properties of encasing antibiotics in polymeric or lipidic nanoparticles show an improvement in infiltration into biofilms, delivery into intracellular pathogens, and reduction of adverse action systemically (van Gent et al. 2021; Ahsan et al. 2024). Nanoparticles also have the ability of reviving already available antibiotics by shielding them against enzymatic breakdown or co-deliver efflux pump inhibitors (Bahader et al. 2024).

Healthcare settings have surface coatings and consumer products that deposit antimicrobial NPs on surfaces with high touch points and in fabrics and catheters to maximize the reduction of the microbial burden (Choudhury et al. 2022). Nanoparticle-based antiviral formulations have been investigated to make protective masks and air-filtration devices who's some have the ability to inactivate

encased viruses at points of contact (Motiei et al. 2023; Tiwari et al. 2023). There is an increase in diagnostic and theragnostic uses: nanoparticles can be used to identify pathogens based on plasmonic sensing, fluorescence, and magnetic separation; multifunctional Nano systems can identify pathogen detection and localized antimicrobial therapy (e.g., bacteria tagged by a sensor layer using photo-thermal ablation) (Saxena et al. 2022).

These efforts at clinical translation have had selective success: a number of topical or device-related NP products utilizing silver or zinc oxide have been launched successfully (Anandapillai et al. 2024). Nevertheless, nanoparticles as antimicrobial agents have fewer regulatory and safety issues when used systemically and fewer clinical trials conducted on a large scale (Elbehiry and Abalkhail 2025).

Safety, toxicity, and environmental concerns

A key issue is safety evaluation. The nanoparticles can interact with mammalian cells and tissues, where they induce inflammatory reactions, oxidative stress, genotoxicity and organ accumulation (Mohamed 2022; Min et al. 2023). The toxicological effect of materials is related to the dose, exposure pathway, and particle permanence (Alijagic et al. 2022). An example is that in extreme cases, silver may be deposited in tissues (resulting in a condition called argyria), and in certain cases, metal oxides release ROS which could damage host cells (Kowalczyk et al. 2021). The protein corona the adsorption of biomolecules to the surface of NPs, regulates bio-distribution and immune-recognition making prediction of in vivo behaviour difficult (Patel and Kanwar 2025). The Eco toxicological issue of consumer products' environmental release is the potential effect of nanoparticles on microbial communities in soil and water, and the impact of which on ecologies and resistance gene propagation is not fully understood (Mubeen et al. 2023). Some risk mitigation measures can be planning biodegradable or easily cleared nanoparticles, control of release kinetics, lower effective doses through synergistic delivery combinations and strict evaluation of life cycle (Ahmad et al. 2022; Bai et al. 2022).

Even though the formation of multimodal mechanisms represents some features that reduce the potential development of single-step mechanisms of resistance in nanoparticles, adaptive mechanisms have been documented (Singh et al. 2022; Sati et al. 2025). To survive exposure to NPs, bacteria can increase efflux pump expression, differentiate cell-surface charge, or develop more thick biofilms (Ngoepe et al. 2025). Use of nanoparticles administered together with antibiotic as a synergy, responsive nanoparticle design to achieve high local concentrations only in the site of infection, rotation or pulsation of nanoparticles, and stewardship of nanoparticles use analogous to antibiotic stewardship are some strategies intended to be used to reduce the development of resistance (Ye et al. 2021; Adeniji et al. 2022).

Antimicrobial nanoparticles need to fulfill regulatory criteria to create an effective, safe, and high-quality capital in translation to clinical application (Parvin et al. 2025). Some of these problems are the standardization of manufacturing with strict control of physicochemical

properties, certain capabilities that are responsive between batches, broad preclinical toxicology (Ahmad et al. 2022). The regulatory routes that are taken during different applications of topical/device or the systemic therapeutic are not similar, and the latter requires longer safety data (Al-Qaysi et al. 2023). The Scale-up should be able to meet the cost, stability, and compatibility with the sterilization type targeted on the medical device or pharmaceuticals (Garvey 2023).

Conclusion

Nanoparticles have emerged as potent antimicrobial agents that offer promising alternatives to conventional antibiotics, which are increasingly challenged by multidrug-resistant microorganisms. Their self-assembled with a great Nano scale and high surface-to-volume ratio makes them have unusual physicochemical characteristics, which causes them to interact with the microbial membranes, proteins and genetic materials. Of all the above nanoparticles, metallic or metal oxide-nanoparticles that include silver, copper, zinc oxide, and titanium dioxide have shown strong bactericidal properties because of their ability to induce three parameters namely reactive oxygen species generation, metal ion release and disruption of the membrane. In the meantime, the polymeric, lipid, and chitosan nanoparticles offer biocompatibility, as well as versatility as targeted in antimicrobial delivery to reverse the side effects of the conventional drugs. The synergizing effects of various types of nanoparticles increase their potential greatness as a therapeutic tool through their hybridization. Despite these merits, there are concerns about the cytotoxicity of nanoparticles, their build-up in the environment, and standardized safety levels. To successfully translate laboratory nanoparticle-microbe interactions, provide the best dosages and exposure time, and produce environmentally acceptable nanoparticles, a better understanding of the nanoparticle-microbe interactions, dosage optimization and exposure time is essential to successful translation laboratory results into practice. Further, the integration of nanotechnology with the regular drug delivery programs, bio sensing and diagnostic equipment can be used to revolutionize the sphere of modern medicine so that it can rapidly identify infection and cure it. In conclusion, the antimicrobial nature of the nanoparticles can be considered a new photo in the biomedical science, which possesses prophylactic and curative possibilities. Necessarily, the manner in which researchers can identify a solution to safe, cost-effective and sustainable nanomaterials would be effective, but put an equilibrium between efficacy and environmental and human safety issues into consideration.

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